Red Book Vaccine Update 2016

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Disclosures

- Member of a Data Safety Monitoring Board, Pfizer
Objectives

• Understand recent trends in US vaccine hesitancy
• Review two new vaccines
  – HPV
  – Meningococcal B
• National Vaccine Plan 2010 to 2020 – How are we doing?
Vaccine Hesitancy
Ten Great Public Health Achievements
United States, 1900 - 1999

- Vaccination
- Motor-vehicle safety
- Safer workplaces
- Control of infectious diseases
- Decline in deaths from coronary heart disease
- Safer and healthier foods
- Healthier mothers and babies
- Family planning
- Fluoridation of drinking water
- Recognition of tobacco use as a health hazard

Source: Center for Disease Control and Prevention, 1999
<table>
<thead>
<tr>
<th>Disease</th>
<th># of Preventable Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>900,000</td>
</tr>
<tr>
<td>Measles</td>
<td>888,000</td>
</tr>
<tr>
<td>Haemophilus influenzae type b (Hib)</td>
<td>400,000</td>
</tr>
<tr>
<td>Pertussis (Whooping cough)</td>
<td>346,000</td>
</tr>
<tr>
<td>Neonatal Tetanus</td>
<td>215,000</td>
</tr>
<tr>
<td>Tetanus</td>
<td>195,000</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>30,000</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>5,000</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>720</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>2,979,720</strong></td>
</tr>
</tbody>
</table>
Vaccine Impact in the US

- Routine immunizations in the US prevent 33,000 child deaths every year
- Vaccine preventable disease reductions of >90%
- Every dollar spent on vaccines in the United States saves $16.50 in medical and societal costs, saving billions of dollars
Estimated Vaccination Coverage, Children 19-35 Months and 13 – 15 years, 1991-2010*

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Coverage</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hib</td>
<td>(3+)</td>
<td></td>
</tr>
<tr>
<td>Hep B</td>
<td>(3+)</td>
<td></td>
</tr>
<tr>
<td>DTP/DTaP</td>
<td>(3+)</td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td>(1+)</td>
<td></td>
</tr>
<tr>
<td>Varicella</td>
<td>(1+)</td>
<td></td>
</tr>
</tbody>
</table>


† Target is 80 percent for Rotavirus, Tdap (1+), MCV4 (1+), HPV (3+) and 90% for varicella (2+)

§ Full series Hib (≥3 or ≥4 doses, depending on product type received). Brand of Hib vaccine received was not collected on the NIS prior to 2009.

¶ Among females
Estimates of Measles-Susceptible Children in the U.S.

- Age-specific measles vaccination data from the National Immunization Survey-Teen used to estimate the number of measles-susceptible children aged 0 to 17 years.

- Approximately **12.5%** of US children and adolescents are currently susceptible to measles.

- Highest levels in children three years and younger (**24.7% susceptible to measles**).

- Sustained decrease in measles vaccination coverage from 91.9% (2013 level) to 90.0% (2009 level) would add nearly 1.2 million susceptible children and adolescents.
  - 14.2% of <17 years and younger would be susceptible to measles.

- Need for high measles vaccination coverage to support population-level immunity and prevent indigenous measles transmission in the United States.

Bednarczyk, Orenstein, Omer, in press 2015; presented at IDWeek, San Diego, 2015.
Estimates of Measles-Susceptible Children in the U.S.

- Projected accumulation of additional susceptible children and adolescents younger than 17 years with a decrease in childhood measles containing vaccine uptake of 2% (relative to 2013 levels), plotted against the decline in the overall proportion of children and adolescents immune to measles.

Bednarczyk, Orenstein, Omer, in press 2015; presented at IDWeek, San Diego, 2015
Understanding Autism

Why More Kids & Families Are Facing the Challenge of ‘Mindblindness’
By Geoffrey Cowley

Parents Wonder: Is it Safe to Vaccinate?
Many families of autistic kids blame the MMR shot for the disorder. Experts say they shouldn’t.
The spread of anti-vax sentiment in California

Share of public school kindergartners with personal belief exemptions to vaccination requirements

Source: California Department of Public Health
California AB 2109

- 2014 documentation requirement for PBE
- Signature that a Health Care Provider has informed parent:
  - Benefits/risks of immunizations
  - Risks to student AND the community
- Kindergarten children with PBEs decreased from 3.15% to 2.54%

http://www.shotsforschool.org/
California SB 277 – No PBEs!

http://www.shotsforschool.org/laws/sb277faq/
Vaccine avoiders put California at risk
29 States Have Introduced Vaccine Bills in 2015

Many would make it harder for parents to opt out of immunizing their kids.

Source: National Vaccine Information Center
“Effective, empathetic communication is critical in responding to parents who are considering not vaccinating their children. Parents should be helped to feel comfortable voicing any concerns or questions they have about vaccination, and providers should be prepared to listen and respond effectively.”

From CDC’s “Providers Guide: Helping Parents Who Question Vaccines”
Human Papillomavirus Vaccines

• Prior to 2015, HPV vaccines contain 2 (HPV bivalent [Cervarix]) or 4 (HPV quadrivalent [Gardasil]) serotypes
  – HPV serotypes 16 and 18 are in both vaccines and are the most common causes of cervical cancer
  – HPV serotypes 6 and 11 are only in HPV4
  – Recommended routinely beginning at 11 years of age

• FDA approval December 2014 of an 9 valent HPV vaccine (HPV9 [Gardasil 9])
  – Approved for use in females ages 9 through 26 and males ages 9 through 15
  – Approved for the prevention of cervical, vulvar, vaginal and anal cancers caused by HPV types 16, 18, 31, 33, 45, 52, 58
  – Approved for the prevention of genital warts caused by HPV types 6 or 11
  – The five additional HPV types in the vaccine (31, 33, 45, 52, 58) cause ~ 20% of cervical cancers
Relative Contribution of HPV Types in HPV9 to Cervical Cancers Worldwide

Lancet Oncol 2010;11:1048-1056
Infect Agent Cancer 2012;7:38
Human Papillomavirus Vaccines

TABLE 1. Characteristics of the three human papillomavirus (HPV) vaccines licensed for use in the United States

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bivalent (2vHPV)*</th>
<th>Quadrivalent (4vHPV)†</th>
<th>9-valent (9vHPV)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand name</td>
<td>Cervarix</td>
<td>Gardasil</td>
<td>Gardasil 9</td>
</tr>
<tr>
<td>VLPs</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>GlaxoSmithKline</td>
<td>Merck and Co., Inc.</td>
<td>Merck and Co., Inc.</td>
</tr>
</tbody>
</table>
Human Papillomavirus Vaccines

- Randomized trial in ~14,000 females 16 through 26 years showed noninferior immunogenicity for types shared by 4vHPV and 9vHPV and high efficacy for the five additional types.

- 9vHPV cost effective when compared with 4vHPV for both sexes
  - Include accounting for HPV natural history, cervical cancer screening, vaccine coverage, vaccine duration of protection, and health care costs
  - Cost effective only based on 9vHPV cost assumptions

- Evidence supporting 9vHPV vaccination deemed type 2 (moderate level of evidence) among females and 3 (low level of evidence) among males
Human Papillomavirus Vaccines

• What are the new recommendations?

• 9vHPV, 4vHPV or 2vHPV can be used for **routine vaccination** of females aged 11 or 12 years and females through age 26 years who have not been vaccinated previously or who have not completed the 3-dose series.

• 9vHPV or 4vHPV can be used for **routine vaccination** of males aged 11 or 12 years and males through age 21 years who have not been vaccinated previously or who have not completed the 3-dose series.

• ACIP **recommends** either 9vHPV or 4vHPV vaccination for men who have sex with men and immunocompromised persons (including those with HIV infection) through age 26 years if not vaccinated previously.
Prevalence of HPV 6, 11, 16, 18 in Cervicovaginal Swabs, NHANES

Prevalence (%)

Age group (years)

14-19
20-24
25-29
30-39
40-49
50-59

2003-2006
2007-2010

56% decline

J Infect Dis 2013;208:385-393
HPV Vaccine Coverage Rates

National Estimated Vaccination Coverage Levels among Adolescents 13-17 Years, NIS-Teen 2006-2012

Source: MMWR. 2013;62;685-93
### Reasons For Parents Not Vaccinating Daughters

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not needed or necessary</td>
<td>19.1%</td>
</tr>
<tr>
<td>Not recommended by provider</td>
<td>14.2%</td>
</tr>
<tr>
<td>Safety concerns / side effects</td>
<td>13.3%</td>
</tr>
<tr>
<td>Lack of knowledge</td>
<td>12.6%</td>
</tr>
<tr>
<td>Not sexually active</td>
<td>10.1%</td>
</tr>
</tbody>
</table>

MMWR 2013;62:591-595
Strength of Recommendations for HPV Vaccination

Current Strength of Recommendation in Females, Pediatricians and Family Physicians (N=609)*

- **11-12 yo females**
  - Strongly recommend: 53%
  - Recommend, but not strongly: 37%
  - Make no recommendation: 8%
  - Recommend against: 2%

- **13-15 yo females**
  - Strongly recommend: 82%
  - Recommend, but not strongly: 15%
  - Make no recommendation: 3%

- **16-18 yo females**
  - Strongly recommend: 87%
  - Recommend, but not strongly: 10%
  - Make no recommendation: 2%

• HPV vaccination often is presented as optional, while other adolescent vaccines are recommended
• Some expressed mixed or negative opinions about the “new” vaccine and concerns over safety/efficacy
• When parents expressed reluctance, physicians were hesitant to engage in discussion
• Some providers shared parents’ views that teen was not at risk for HPV and could delay vaccination until older
Actual and potentially achievable vaccination coverage of ≥1 HPV among adolescent girls if missed opportunities* were eliminated, NIS-Teen

Among unvaccinated girls, 84% had a missed opportunity for HPV

*Missed opportunity defined as having a healthcare encounter where at least one vaccine was administered but HPV was not

MMWR. 2013; 62:591-5
HPV Transmission

- HPV exposure can occur with any type of intimate sexual contact
- Among a cohort of adolescent women without prior vaginal intercourse (followed longitudinally)
  - HPV was detected in 46% of females prior to 1st vaginal sex
  - 70% of these women reported non-coital behaviors that may in part explain genital transmission
- Vaginal intercourse is **not** necessary to become infected
- Condoms do not completely stop HPV transmission

Three main strains of *Neisseria meningitidis* (meningococcus) circulate in the United States – Serogroups B, C, and Y

Serogroup B disease is common in young children and becoming more common in adolescents and adults

*N. meningitidis* causes overwhelming sepsis and meningitis with a high mortality rate (approximately 10%)

The previously licensed meningococcal vaccines contain serogroup A, C, Y, and W
Meningococcal Disease

Meningococcal Incidence in All Ages by Serogroup and Adolescent MenACWY Vaccine Coverage, 1993–2013

- Serogroup B
- Serogroup C
- Serogroup Y

2013: 564 cases\(^3\) (0.18/100,000)
2013 MenACWY coverage, NIS-Teen\(^2\):
- \(\geq 1\) dose: 77.8% (range by state, 40.4%-93.7%)
- 2 dose completion: 29.6%

Source: Active Bacterial Core surveillance (ABCs) cases from 1993-2013 estimated to the U.S. population with 18% correction for nonculture confirmed cases. In 2010, estimated case counts from ABCs were lower than cases reported to the National Notifiable Diseases Surveillance System (NNDSS) and might not be representative.


\(^3\)NNDSS 2013 final case count
Meningococcal Disease

Work Group Interpretation: Burden of Disease

- Incidence of disease has declined for all meningococcal serogroups, including serogroup B
  - Currently at a stable low in disease incidence

- Approximately 55–65 cases of serogroup B meningococcal disease occur in adolescents and young adults each year
  - The majority of those cases occur in older adolescents and young adults aged 16–24 years

- Approximately 40-70% of serogroup B cases in 18–23 year olds occur in college students
  - Incidence in college and non-college students is similar
Two MenB Vaccines For Persons Aged 10–25 Years in the United States

- **MenB-FHbp (Trumenba®, Pfizer)**
  - Components: fHbp subfamily A/v2,3; subfamily B/v1
  - 3 dose series, administered at 0, 2, 6 months
  - Licensed in the U.S. on October 29, 2014

- **MenB-4C (Bexsero®, Novartis/GSK)**
  - Components: fHbp subfamily B/v1, Nhba, NadA, Por A1.4
  - 2 dose series, administered at 0 and ≥1 month
  - Licensed in the U.S. on January 23, 2015
  - Licensed in >37 countries for persons ≥2 months of age
Meningococcal Disease

Work Group Interpretation: Immunogenicity

- Immunogenicity suggests short term efficacy
- Evidence of waning antibody levels within 6 months post dose 3 for MenB-FHbp
  - Appears to stabilize 6-48 months post dose 3
- Modest waning in antibody observed through 24 months post dose 2 for MenB-4C
  - Data from Chilean adolescents with higher baseline bactericidal antibodies compared to U.S. adolescents
- Proportion of vaccinees who develop bactericidal antibodies may vary with each outbreak or circulating strain
### Meningococcal Serogroup B Vaccines

#### Potential Cases and Deaths Prevented per 4M Cohort

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Cases Prevented</th>
<th>Deaths Prevented</th>
<th>NNV* to prevent case</th>
<th>NNV to prevent death</th>
<th>Cost ($) per QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series at 11 years</td>
<td>15</td>
<td>2</td>
<td>203,000</td>
<td>1,512,000</td>
<td>$8,700,000</td>
</tr>
<tr>
<td>Series at 16 years</td>
<td>28</td>
<td>5</td>
<td>107,000</td>
<td>788,000</td>
<td>$4,100,000</td>
</tr>
<tr>
<td>Series at 18 years</td>
<td>29</td>
<td>5</td>
<td>102,000</td>
<td>638,000</td>
<td>$3,700,000</td>
</tr>
<tr>
<td>College students</td>
<td>9</td>
<td>1</td>
<td>368,000</td>
<td>2,297,000</td>
<td>$9,400,000</td>
</tr>
</tbody>
</table>

*Number needed to vaccinate

Source: Israel Ortega Sanchez
Meningococcal Disease

Considerations for Category B Rather Than Category A Recommendation

- **Current low burden of disease**
  - Number needed to vaccinate to prevent a case/death is high
  - Number of cases prevented may be comparable to the number of serious adverse reactions to vaccine

- **Additional data to consider routine recommendations is needed**
  - Understanding the true proportion of serogroup B cases that could be prevented with MenB vaccines
    - Vaccine effectiveness and duration of protection
    - Impact on carriage and herd immunity
ACIP Deliberations – Meningococcal B Vaccine

- The current low prevalence of disease, coupled with the fact that important data for making policy recommendations for MenB vaccines are not yet available, resulted in ACIP determining that insufficient evidence exists to make a routine public health recommendation that all adolescents be vaccinated with MenB vaccine.

- Given the seriousness of meningococcal disease and the availability of licensed vaccines, ACIP agreed that sufficient evidence exists to encourage individual clinical decision making.

- American Academy of Pediatrics in agreement with ACIP policy.
CDC Recommendations for Meningococcal B Vaccine

What is currently recommended?

- ACIP recommends routine vaccination of all adolescents aged 11–18 years with a quadrivalent meningococcal conjugate vaccine (MenACWY)
- A single dose at age 11 or 12 years with a booster dose at 16 years for persons who receive the first dose before age 16 years.

Why are the recommendations being modified?

- Two serogroup B meningococcal vaccines licensed by the FDA for use in persons aged 10–25 years.
- Recommendation was Category B (recommended for individual clinical decision making)

What are the new recommendations?

- A MenB vaccine series may be administered to adolescents and young adults aged 16–23 years to provide short-term protection against most strains of serogroup B meningococcal disease. The preferred age for MenB vaccination is 16–18 years.
- Routine vaccination of certain persons at increased risk for meningococcal disease with MenACWY and serogroup B meningococcal (MenB) vaccine is also recommended.
Mid-course Review of the 2010 National Vaccine Plan
U.S. Vaccine and Immunization Ecosystem
2010 National Vaccine Plan

Goal 1: Develop new and improved vaccines

Goal 2: Enhance the vaccine safety system

Goal 3: Support communications to enhance informed vaccine decision-making

Goal 4: Ensure a stable supply of, access to, and better use of recommended vaccines in the United States

Goal 5: Increase global prevention of death and disease through safe and effective vaccination
### National Vaccine Plan Priorities for Implementation

<table>
<thead>
<tr>
<th>A.</th>
<th>Develop a catalogue of priority vaccine targets of domestic and global health importance (Goal 1).</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.</td>
<td>Strengthen the science base for the development and licensure of new vaccines (Goals 1 and 2).</td>
</tr>
<tr>
<td>C.</td>
<td>Enhance timely detection and verification of vaccine safety signals and develop a vaccine safety scientific agenda (Goal 2).</td>
</tr>
<tr>
<td>D.</td>
<td>Increase awareness of vaccines, vaccine-preventable diseases, and the benefits/risks of immunization among the public, providers, and other stakeholders (Goal 3).</td>
</tr>
<tr>
<td>E.</td>
<td>Use evidence-based science to enhance vaccine-preventable disease surveillance, measurement of vaccine coverage, and measurement of vaccine effectiveness (Goal 4).</td>
</tr>
<tr>
<td>F.</td>
<td>Eliminate financial barriers for providers and consumers to facilitate access to routinely recommended vaccines (Goal 4).</td>
</tr>
<tr>
<td>G.</td>
<td>Create an adequate and stable supply of routinely recommended vaccines and vaccines for public health preparedness (Goal 4).</td>
</tr>
<tr>
<td>H.</td>
<td>Increase and improve the use of interoperable health information technology and electronic health records (Goal 4).</td>
</tr>
<tr>
<td>I.</td>
<td>Improve global surveillance for vaccine-preventable diseases and strengthen global health information systems to monitor vaccine coverage, effectiveness, and safety (Goal 5).</td>
</tr>
<tr>
<td>J.</td>
<td>Support global introduction and availability of new and under-utilized vaccines to prevent diseases of public health importance (Goal 5).</td>
</tr>
</tbody>
</table>

Priorities identified to guide federal immunization efforts across government agencies
Why Conduct a Mid-course Review?

2010 National Vaccine Plan:

“Recognizing these uncertainties, NVPO will coordinate a mid-course review of the Plan after five years allowing changes to be made which respond to the reality of the environment. Modified indicators, strategies, actions, and milestones will guide subsequent annual evaluation through the overall ten-year horizon of the Plan.”
Why Conduct a Mid-course Review?

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To guide development of 2016-2020 Implementation Plan

• outline near-term, actionable efforts based on areas where we have the greatest opportunity to move the program forward by 2020

To serve as a framework for building community consensus on priorities areas

• Where progress has been made, where it is needed, and what is possible by 2020

To serve as a roadmap for incoming political leaders

• Clearly-defined priorities laid out across the vaccine ecosystem can aid incoming political leaders in decisions that could impact resource allocation
Questions Framing the Mid-course Review

- Broadly speaking, is the Plan meeting its goals and objectives?
- Based on the current landscape, are we still going in the direction needed?
- How do we optimize implementation efforts going forward to better align with the current immunization landscape?
  - How will we ensure coordination with other vaccine and immunization-focused strategic plans across the Department?
- How will we measure our progress? How will we know we reach our near-term goals (i.e., how will we define success)?
2010 NVP Mid-course Review

- Multi-pronged approach to solicit input from both federal and non-federal stakeholders
  - Federal data-call and non-federal RFI (Oct 2015)
  - One-on-one interviews (federal and non-federal partners)
  - Small group interviews
  - Focus groups (federal and non-federal partners)
  - Interagency calls for information sharing

- Building consensus and stakeholder support around the greatest areas of opportunity for accomplishing our NVP goals in the next five years

- Frequent engagement with federal partners to verify accomplishments, to gain further input on prioritized opportunity areas, and to identify metrics
  - One-on-one interviews with federal agencies

- All results also provided to the NVAC Working Group for deliberation and discussion—separate analysis and recommendations
1) Strengthen the health information system to track, analyze, and visualize disease, vaccine coverage, and safety data

2) Foster and facilitate efforts to strengthen confidence in vaccines and the immunization system to increase coverage across the lifespan

3) Eliminate financial and systems barriers for providers and consumers to facilitate access to and administration of routinely recommended vaccines

4) Strengthen the science base for the development and licensure of new vaccines, especially our understanding of the host immune system and correlates of protection

5) Identify and implement solutions to overcome vaccine development barriers
Take Home Points

- Continued emphasis on routine immunizations to provide broad herd immunity, especially for highly contagious diseases such as measles
- New HPV9 vaccine now available, providing broader serotype protection
- We need to do a better job of delivering HPV vaccine to adolescents.
- Serogroup B meningococcal vaccine now available with recommendations for limited use
- The National Vaccine Plan 2010-2020 is on track but many new opportunities to improve vaccination and health in all US populations exist
References/Resources

- NNII (www.immunizationinfo.org)
- VEC (www.vaccine.chop.edu)
- IAC (www.immunize.org)
- CDC/NIP (www.cdc.gov/nip)
- http://www.cdc.gov/meningococcal
- AAP (www.aap.org)
- AAFP (www.aafp.org/)
- IVS (www.vaccinesafety.edu)
- Vaccine Page (www.vaccines.org)
- Every Child by Two (www.ecbt.org)
- PKIDS (www.pkids.org/)

http://www.cdc.gov/vaccines/acip/meetings/slides-2014-06.html
http://www.cdc.gov/measles/travelers.html
Thank you

Questions?

WE DID IT!
SB277 is law.
Thank You

#sb277  #vaccineswork  vaccinatecalifornia.org
CDC Recommendations for Meningococcal B Vaccine

• Meningococcal B vaccine series **MAY** be administered to adolescents and young adults aged 16-23 years to provide short-term protection against most strains of serogroup B meningococcal disease (recommendation category B)

• Routine use (recommendation category A) in certain groups at increased risk for serogroup B meningococcal disease, including during outbreaks

  – people with persistent complement component diseases, including inherited or chronic deficiencies in C3, C5-C9, properdin, factor D, or factor H
  – people receiving eculizumab (Soliris, Alexion Pharmaceuticals Inc, Cheshire, CT), a monoclonal antibody that acts as a terminal complement inhibitor by binding C5 and inhibiting cleavage of C5 to C5A
  – people with anatomic or functional asplenia, including sickle cell disease
  – healthy people at increased risk because of a serogroup B meningococcal disease outbreak